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Gynecological Cancers And Vital Substances

Current Research Work

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This article deals with cancers of the breast, ovaries, uterus and cervix. The focus is on nutrition including micronutrients, the gut microbiome, frailty, bone resorption, tumor microenvironment and cervical HPV infection.

The Role Of The Gut Microbiome

The gut microbiome plays a crucial role in influencing cancer progression and response to treatments.

Probiotics
A systematic review and meta-analysis included 15 studies with a total of 2,197 participants. Probiotics significantly reduced the incidence of chemotherapy-induced diarrhea in moderate heterogeneity. This underlines their potential as a supportive therapy option in oncology [1].

Fiber
The gut microbiome is significantly influenced by diet. Higher fiber intake from fruits, vegetables, and whole grains is associated with a lower risk of breast cancer-specific and general mortality, as

well as reduced colorectal cancer-specific mortality. Higher consumption of nuts is associated with improved disease-free survival in patients with breast, colorectal and prostate cancer. Soy is considered safe for breast cancer patients and is associated with a reduced risk of recurrence [2].
A meta-analysis included 9 case-control studies with sample sizes between 120 and 851 and an age range of 18 to 75 years. The pooled results showed an inverse, thus a reverse, relationship between the DPI (Dietary Phytochemical Index) and the risk of all types of cancer. The DPI determines the intake of foods with a high phytochemical density, e.g. whole grains, fruits, vegetables, nuts and legumes. Furthermore, a subgroup analysis proved that a higher DPI score is associated with a lower risk of breast cancer, etc. [3].

Mediterranean Diet
A systematic review and meta-analysis of 17 studies involving 23 to 6,457 subjects proved that stricter adherence to the Mediterranean diet (MD) was associated with lower all-cause mortality in cancer patients and a higher quality of life. This was also true for subgroups with ovarian and breast cancer, among others. With respect to improved disease-free survival in breast cancer patients the evidence was moderate [4].

Accompanying Symptoms Of Gynecological Cancers

Frailty, nutrient deficiency and anemia often occur together in gynecological cancers and can negatively influence the clinical course. 180 patients (endometrium n = 72, ovary n = 71, vulva n = 26, cervix n = 6, vagina n = 5; mean age 69.6 ±7.9 years; follow-up 25.1 ± 16.3 months) who underwent gyneco-oncological surgery were prospectively examined for frailty.

The G8 score (G8) served as a geriatric screening tool: G8-positive patients (≤14 points) had more comorbidities and were more likely to have preoperative anemia, hypoalbuminemia, as well as **vitamin D or B12 deficiency.** FIGO stages, surgical approach, and postoperative complications were comparable. G8-positive patients were less likely to receive standard adjuvant therapy.

Conclusion: A low preoperative G8 score was associated with a reduced progression-free and potentially worse overall survival rate in older women with gynecological tumors. The G8 tool can help detect modifiable factors such as anemia or vitamin D deficiencies, while complete tumor resection remained the most significant prognostic factor, according to a German study [5].

Vitamin D Levels And Cancer

A total of 13 studies involving 2,592 cancer patients were included in a systematic review and meta-analysis. Higher vitamin D concentrations were associated with improved overall survival, better progression-free survival, event-free survival, and objective response rates. All included patients with solid tumors received immune checkpoint inhibitors and showed positive effects from higher vitamin D levels. In addition, a significant correlation between vitamin D intake and longer overall survival was observed [6].

Briefly Explained

- **G8 Score:** The aim of the G8 is to rapidly screen older cancer patients to identify those for whom a full Comprehensive Geriatric Assessment (CGA) is indicated. A cut-off <14/17 points indicates potential vulnerability. The Comprehensive Geriatric Assessment (CGA) is used to systematically record the following dimensions: functional status, mobility, cognition, nutritional status, comorbidities, polypharmacy, psychosocial aspects.
- **FIGO Stages:** The FIGO classification describes how far an endometrial carcinoma has spread and whether there are metastases. The FIGO classification distinguishes between four stages.

Breast Cancer

Breast cancer, for a long time the most common cause of cancer-related death in women, has now fallen back to second place. Lung cancer is now at the top for the first time [7].

Dietary Supplement

The use of dietary supplements is common in women with breast cancer, but there is a lack of reliable evidence of benefit or harm.

In a Danish cohort study with 1,951 breast cancer cases, the intake of food supplements before and after diagnosis was investigated and followed for up to 20 years. During follow-up (median 12 years), 725 women died, 450 of whom died of breast cancer. For the general use of food supplements, there was no association with life expectancy. However, multivitamins were associated with a slightly longer survival time (approx. +1 year). On the other hand, indications showed a shortened life expectancy with a high intake of vitamin A, B12, iron, magnesium and with very low or high vitamin D intake. Antioxidant food supplements could be disadvantageous during chemotherapy, but not during radiotherapy. Recommended intake levels should not be exceeded [8].

A total of 45 randomized, controlled studies were included in a systematic review. Vitamin D supplementation revealed promising results in some studies with potential immunomodulatory and antioxidant effects, especially when combined with other interventions. Omega-3 fatty acids and beta-glucans showed potential in alleviating certain symptoms and improving quality of life. Beta-glucans had potential immune-stimulating effects. Overall, supplementation of food supplements was not associated with serious side effects in the included studies [9].

A possible source of these nutrients is, for example, Unizink® IMMUN PLUS capsules - with zinc, selenium, beta-(1.3/1.6)-glucan, vitamins C, D3, E and citrus bioflavonoids.

Breast Cancer And Vitamin D

Insufficient vitamin D levels were common in women with breast cancer (BC), as was impaired muscle strength (MS). An observational cross-sectional study was conducted in 151 adult women with breast cancer without metastases or recurrence within up to twelve months after diagnosis.

The serum 25(OH)D concentration was categorized as either inadequate (< 30 ng/ml) or sufficient (≥ 30 ng/ml). Muscle strength was assessed by hand gripping force test and divided into tertiles of the study population: 1st tertile (6 to 21 kg), 2nd tertile (22 to 26 kg) and 3rd tertile (27 to 39 kg). The majority of the subjects (70%) had insufficient serum vitamin D levels associated with the 1st and 2nd muscle strength tertiles. An insufficient vitamin D serum concentration thus significantly increased the likelihood of impaired muscle strength [10].
A review dealt with the complex interplay between vitamin D, butyrate and breast cancer. Fat-soluble vitamin D is involved in the development, progression and prognosis of breast cancer, but its exact mechanisms of action remain difficult to determine. The latest findings from basic and clinical research indicate that vitamin D is activated by hydroxylases and thus the active form $1,25(OH)_2D$ is formed, which can increase the amount of butyrate-producing bacteria. The short-chain fatty acid butyrate, in turn, can regulate the intestinal microenvironment and modulate the immune system in order to inhibit the proliferation of breast cancer cells. These findings open up promising perspectives for innovative clinical approaches in breast cancer therapy [11].

The **tumor microenvironment (TME) in breast cancer** consists of different cell types, the extracellular matrix, and other components that promote tumor growth and metastasis. Vitamin D is considered a potential protective factor against breast cancer and shows antitumor effects, such as influencing cell cycle, differentiation, apoptosis, angiogenesis, and metastasis. While these effects are well studied, up to now the direct influence of vitamin D on the tumor microenvironment has been poorly analyzed. A review comprehensively presents the anticarcinogenic mechanisms of vitamin D in the context of TME in breast cancer, including its regulatory effect on cancer-associated fibroblasts, adipocytes, immune cells, cancer stem cells, and the extracellular matrix. This highlights the potential of vitamin D to specifically reprogram TME and improve the efficacy of existing breast cancer therapies [12].

Breast Cancer And Selenium Status
In patients on neoadjuvant chemotherapy (NAC), a pathologically complete response (pCR) shows a high survival rate. While tumor factors are well studied, there is little data on patient factors.
In a study with 329 women with HER2-positive (n = 183) or triple-negative breast cancer (n = 146), the selenium concentration in the blood was determined and divided into tertiles before the start of NAC. Subsequently, the achievement of a pCR was assessed. Result: The pCR rate was 59.0% in the highest selenium tertile (≥ 107.19 µg/I) compared to 39.0% in the lowest (≤ 94.29 µg/l).

Conclusion: High selenium levels could be a predictor of pCR. Further studies should examine whether selenium supplements improve treatment success and survival [13].
The trace element selenium plays an important role in cancer biology, especially in breast cancer. Studies show that it can have both antioxidant and prooxidative effects, depending on its concentration. As a result, it influences central signaling pathways that control apoptosis and cell proliferation.

Selenium regulates oxidative stress and contributes to the balance between cell survival and programmed cell death. In breast cancer cells, it can trigger apoptosis, for example through mitochondrial processes, caspase activation as well as the regulation of genes such as p53, Bax and BcI-2. At the same time, it inhibits tumor growth by stopping the cell cycle and suppressing important signaling pathways.
These properties make selenium a potentially promising approach in cancer prevention and therapy, especially in combination with other treatments. However, due to possible opposing effects at high doses, careful dosing is necessary [14]. Individual dosing of selenium is possible, for example, Uniselen 100 NE and Uniselen 200 NE.

Cervical Cancer

Cervical cancer is the fourth most common cancer in women, with an advanced mortality rate of about 50% (in 2020).

Vitamin D

Studies suggest that vitamin D3 (cholecalciferol) may affect the growth of cancer cells.
In a randomized trial of 123 patients with advanced cervical cancer, they received either 10,000 IU of vitamin D3 daily or a placebo during and after radiation therapy. Three months after treatment, the vitamin D group showed a higher complete remission rate (82.61% vs. 64.8%) as well as higher median serum vitamin D levels.
The results suggest that vitamin D3 can positively support therapy in advanced cervical cancer and possibly promote cancer-free survival [15].

CIN And Folic Acid

Folate plays an important role in one-carbon metabolism and affects DNA synthesis and methylation.
A meta-analysis of 25 studies with 14,304 participants showed that low folate levels (serum and red blood cells) are associated with an increased risk of cervical intraepithelial neoplasms (CIN) and/or cervical cancer. An additional folic acid intake of 240 to 280.5 µg/day was associated with a risk reduction of up to 26%. In addition, higher folate levels in serum and erythrocytes led to a further risk reduction. Regression of CIN was also associated with folic acid supplementation.

Conclusion: A higher folic acid intake and better folate levels could reduce the risk of CIN and cervical cancer and are therefore relevant for prevention [16].

HPV Infections And Zinc

Chronic infections with the human papillomavirus (HPV) are a major cause of cervical intraepithelial neoplasia (CIN) and cervical cancer.

Scientists investigated the efficacy of oral zinc and a topical nitrate-zinc complex solution (NZCS) in viral warts as well as in cervical HPV infection and associated lesions. A total of 33 clinical trials involving 2,728 patients were included in the systematic review and meta-analysis. Zinc showed significant efficacy in eliminating cervical HPV infections. The results suggest that zinc compounds and NZCS are effective and safe treatment options for patients with viral warts and cervical HPV infection [17].

Uterine (Body) Cancer And Oxidative Stress

Oxidative stress is associated with the development of gynecological cancers, including endometrial cancer. In one study, 200 patients were compared with 200 healthy women. Cancer patients showed significantly lower levels of **antioxidants such as vitamin C and glutathione,** while markers of oxidative stress were elevated. In addition, there was an inverse relationship between antioxidants and oxidative markers. Low levels of glutathione and vitamin C were independently associated with an increased risk of disease. The results suggest that a redox imbalance plays an important role in the development of endometrial cancer and could contribute to early detection [18].

Ovarian Cancer

Bone Resorption In Ovarian Cancer

Ovarian cancer can lead to bone loss. Three main factors put a strain on bone health:

- the hormonal change after the operation,
- the activation of the osteoclasts by the tumor and
- harmful effects of chemotherapy.

Despite the high risk, bone health is often not adequately monitored. DXA measurement is the most important diagnostic procedure, supplemented by other methods for fracture risk assessment. Medications such as bisphosphonates or denosumab, as well as calcium, vitamin D, exercise and fall prevention can help [19].

Integrative Oncological Measures For Ovarian Cancer

A biochemical recurrence of epithelial ovarian cancer (EOC) is manifested by rising CA-125 levels without clinical findings. Early cytotoxic therapy does not improve survival and can worsen quality of life. Integrative oncological measures can support this: Mind-body procedures such as mindfulness, yoga and cognitive behavioral therapy reduce anxiety and stress. Exercise and acupuncture promote vitality, mood and sleep. An **anti-inflammatory diet, sufficient vitamin D supply and omega-3 fatty acids** promote resilience and general health. Natural substances such as green tea, medicinal mushrooms, modified citrus pectin, melatonin and Active Hexose Correlated Compound (AHCC: mycelium extract from the shiitake mushroom) show immunomodulating or antitumor effects in preclinical or early clinical studies. Overall, these approaches are considered safe and, above all, they improve the quality of life [20].

Conclusion

Therapists may be able to use this knowledge to encourage their patients to adopt a healthy or healthier lifestyle, which can contribute to a better prognosis. Micronutrients should only be supplemented if the levels are not within the normal range. For vitamin D, the evidence currently seems to be the best.

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Keywords: breast cancer, gut microbiome, gynecological cancers, micronutrients, vitamin D.

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The Author



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Until 2003, the naturopath ran her own practice for classical homeopathy and nutritional counselling. Since 2002, she has been a freelance author for various naturopathic journals and prefers to write about phytotherapy, nutrition, oncology, environmental medicine and orthomolecular medicine.

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